



UNITED STATES DEPARTMENT OF COMMERCE  
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**NOTICE OF ALLOWANCE AND ISSUE FEE DUE**

HM31/0428

FOLEY & LARDNER  
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WASHINGTON DC 20007-5109

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
07/943,246	09/10/92	020	CROUCH, D	1632 04/28/98
First Named Applicant	LUBON, HENRYK			

TITLE OF INVENTION: EXPRESSION OF ACTIVE HUMAN PROTEIN C IN MAMMARY TISSUE OF TRANSGENIC NON-HUMAN MAMMALS USING A LONG WAP PROMOTOER (AS AMENDED)

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1 30523/105	800-002.000	D55	UTILITY	NO	\$1320.00	07/28/98

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

**HOW TO RESPOND TO THIS NOTICE:**

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

- A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
- B. If the status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

- A. Pay FEE DUE shown above, or
- B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "4b" of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give application number and batch number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

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07943246 07943246 LUBON FIRST NAMED APPLICANT H 005237105

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HM31/0422

EXAMINER  
CROUCH, D

ABT UNIT PAPER NUMBER  
1632

43/12  
04/22/98

DATE MAILED:

NOTICE OF ALLOWABILITY

PART I

- ☒ This communication is responsive to the response filed March 24, 1998
- ☒ All the claims being allowable. PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice Of Allowance And Issue Fee Due or other appropriate communication will be sent in due course.
- ☒ The allowed claims are 1-4, 6-9, 11, 13 and 16-24 renumbered as given below
- ☐ The drawings filed on \_\_\_\_\_ are acceptable.
- ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has [...] been received. [...] not been received. [...] been filed in parent application Serial No. \_\_\_\_\_, filed on \_\_\_\_\_.
- ☒ Note the attached Examiner's Amendment.
- ☒ Note the attached Examiner Interview Summary Record, PTOL-413.
- ☒ Note the attached Examiner's Statement of Reasons for Allowance.
- ☐ Note the attached NOTICE OF REFERENCES CITED, PTO-892.
- ☐ Note the attached INFORMATION DISCLOSURE CITATION, PTO-1449.

PART II

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" indicated on this form. Failure to timely comply will result in the ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
- ☒ APPLICANT MUST MAKE THE DRAWING CHANGES INDICATED BELOW IN THE MANNER SET FORTH ON THE REVERSE SIDE OF THIS PAPER.
  - ☒ Drawing informalities are indicated on the NOTICE RE PATENT DRAWINGS, PTO-948, attached hereto or to Paper No. 8. CORRECTION IS REQUIRED.
  - ☐ The proposed drawing correction filed on \_\_\_\_\_ has been approved by the examiner. CORRECTION IS REQUIRED.
  - ☐ Approved drawing corrections are described by the examiner in the attached EXAMINER'S AMENDMENT. CORRECTION IS REQUIRED.
  - ☒ Formal drawings are now REQUIRED.

Any response to this letter should include in the upper right hand corner, the following information from the NOTICE OF ALLOWANCE AND ISSUE FEE DUE: ISSUE BATCH NUMBER, DATE OF THE NOTICE OF ALLOWANCE, AND SERIAL NUMBER.

Attachments:

- ☒ Examiner's Amendment
- ☒ Examiner Interview Summary Record, PTOL-413
- ☒ Reasons for Allowance
- ☐ Notice of References Cited, PTO-892
- ☐ Information Disclosure Citation, PTO-1449

- ☐ Notice of Informal Application, PTO-152
- ☐ Notice re Patent Drawings, PTO-948
- ☐ Listing of Bonded Draftsmen
- ☐ Other

04/23/1998 DBEACH 00000006 190741 07943246  
01 FC:217 275.00 CH

original allowed  
1 = 1  
2 = 2  
3 = 3  
4 = 4  
6 = 5  
7 = 6  
8 = 7  
9 = 8  
11 = 9  
12 = 15  
14 = 10  
16 = 20

original allowed  
12 = 16  
18 = 17  
19 = 18  
20 = 19  
21 = 11  
22 = 12  
23 = 13  
24 = 14

An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on April 21, 1998, Mr. Stephen Bent requested an extension of time for one MONTH(S) and authorized the Commissioner to charge Deposit Account No. 19-0741 the required fee of \$275.00 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Please enter the following amendments:

1. In claim 1, line 2, delete "an exogenous" and insert --a--.
2. In claim 1, line 3, delete "exogenous".
3. In claim 1, line 5, before "protein" insert --a heterologous--.
4. In claim 4, line 2, delete "exogenous".
5. In claim 6, line 1, insert --heterologous-- before "production".
6. In claim 6 (A), lines 1-5, delete "providing .... protein C", and insert --providing a non-human transgenic mammal whose genome comprises a stably integrated DNA sequence comprising the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene, operably linked to a DNA sequence encoding a heterologous protein C--.
7. In claim 6 (B), lines 2 and 3, delete "secreted".
8. In claim 9, line 2, delete "exogenous".
9. In claim 12, line 2, insert -heterologous- before "polypeptide".
10. In claim 12 (A), lines 1-5, delete "providing .... protein C", and insert --providing a non-human transgenic mammal whose genome comprises a stably integrated DNA sequence comprising the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene, operably linked to a DNA sequence encoding a heterologous <sup>polypeptide</sup> protein C--.
11. In claim 12 (B), line 2, delete "secreted".

12. In claim 14, line 2, delete "an exogenous" and insert --a--.
13. In claim 14, line 3, delete "exogenous".
14. In claim 14, line 5, after "DNA" insert --sequence--.
15. In claim 14, line 5, before "polypeptide", insert --heterologous".
16. In claims 22, 23 and 24, delete "process" and insert "mammal".
17. In the abstract, page 57, lines 5 and 7, delete "animals" and insert --non-human mammals--, and line 10 delete "animal" and insert --non-human mammal--..

The following is an examiner's statement of reasons for allowance: The production of transgenic non-human mice, rats, rabbits, pigs, sheep, goats and cows that comprised the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene operably linked to a DNA sequence encoding a heterologous protein and expressed protein C in their milk was seen as predictable by the showing in the specification of transgenic mouse (specification, pages 46-50) and, in the declaration filed (copy) January 10, 1994 as an attachment to paper 10 of transgenic pigs (exhibit 7 and specification pages 28-29). This showing of protein C production was seen a predictive of the production of transgenic non-human mice, rats, rabbits, pigs, sheep and goats that comprised the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene operably linked to a DNA sequence encoding a heterologous protein. The arguments submitted in the response file March 24, 1998 as whole were persuasive regarding the enablement of transgenic cows expressing any transgene from the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene. In particular, arguments directed to WO 91/08216 published June 13, 1991 (especially example 7) Kimpenfort et al (1991) Bio/Technology 9, 844-847 (see especially materials and methods) and the abstract by Nuijens et al dated February 1997 (exhibit 1, filed 3/24/98) demonstrated a trail from the first production of transgenic bovine embryos to transgenic cows which produced detectable quantities of lactoferrin in their milk. Thus the art recognized

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Art Unit: 1632

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an evolution in data which resulted in a reasonable predication of producing a transgenic cow that would produce a protein from the promoter as claimed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

The fax number is (703) 308-4242.

Please note the change in art unit number to Art Unit 1632. Please use this art unit number on all correspondence.

*Deborah Crouch*

Dr. D. Crouch  
April 21, 1998

DEBORAH CROUCH  
PRIMARY EXAMINER  
~~GROUP 1800~~

*Tech. Cent. 1600*